UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/758,644	01/15/2004	Peter Wernet	07588/026003	5815

21559 7590 07/01/2008

CLARK & ELBING LLP
101 FEDERAL STREET
BOSTON, MA 02110

EXAMINER	
NGUYEN, QUANG	

ART UNIT	PAPER NUMBER
1633	

NOTIFICATION DATE	DELIVERY MODE
07/01/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentadministrator@clarkelbing.com

Office Action Summary	Application No.	Applicant(s)	
	10/758,644	WERNET, PETER	
	Examiner	Art Unit	
	QUANG NGUYEN, Ph.D.	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 April 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 2* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 2* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/16/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment filed on 4/7/08 was entered.

Claims 1-2 are pending in the present application, and they are examined on the merits herein.

Claim Objections

Claim 2 is objected to because the phrase "said USSCs are isolated from umbilical cord blood or are obtained from USSCs isolated from umbilical cord blood" is redundant. Appropriate correction is required.

Response to Applicant's remark

Applicant does not believe the objection is warranted and does not know of an amendment that could be made that would address the objection.

It is noted that "said USSCs are isolated from umbilical cord blood" and "said USSCs are obtained from USSCs isolated from umbilical cord blood" refer to he same or identical USSCs. Therefore, the phrase is redundant. To overcome this objection, the claim should recite simply - - said USSCs are isolated from umbilical cord blood - -.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-2 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pittenger et al. (WO 99/03973) in view of either Bruder et al (WO 97/39104; Cited previously) or Abatangelo et al. (US 6,482,231B1) as evidenced by Ha et al. (US 2005/0118714 A1) for the same reasons already set forth in the Office action mailed on 11/08/07 (pages 3-5). ***The same rejection is restated below***

Pittenger et al already disclose a method of administering to the heart of an individual a cardiomyocyte producing amount of human mesenchymal stem cells to regenerate or repair striated cardiac muscle that has been damaged through disease or degeneration, such as ischemic hearts and congestive heart failure patients (see at least Summary of the Invention, pages 2-4).

Pittenger et al does not teach specifically the use of human mesenchymal stem cells that are obtained from umbilical cord blood.

However, at least at the filing date of the present application Bruder et al. already taught a cryopreserved preparation comprising an isolated, homogenous population of viable **human mesenchymal stem cells** for human clinical use, and the mesenchymal cells are obtained from periosteum, bone marrow, ***cord blood***, peripheral blood, dermis, muscle or other known sources of mesenchymal stem cells (see at least page 3, second and fourth paragraph; page 6, last paragraph). In an exemplification, Bruder et al disclosed that the mesenchymal stem cells can be culturally expanded, for example, in BGJb medium containing 10% fetal serum or in any chemically defined

medium (page 3, third paragraph). The exemplified isolating method includes the steps: a Percoll gradient fractionating step to obtain a low density fraction, plating collected cells in the Petri dish for selective separation based upon cell adherence of hMSCs and the removal of non-adherent cells (page 12, second paragraph continues to page 13).

At the effective filing date of the present application, Abatangelo et al also taught the use of **a biological material comprising a cell preparation enriched in or isolated homogenous population of human mesenchymal stem cells obtained from various sources including umbilical cord, placenta** and others for therapeutic methods in an individual in need thereof (see at least Summary of the Invention; col. 2, lines 32-46; col. 5, line 58 continues to line 8 of col. 6; col. 7, lines 28-60; claims 1-5 and 15-16).

It would have been obvious for an ordinary skilled artisan to modify the teachings of Pittenger et al by also **using the cord blood-derived mesenchymal stem cells** to regenerate or repair striated cardiac muscle that has been damaged through disease or degeneration in a patient in need thereof, in light of the teachings of either Bruder et al. or Abatangelo et al. The isolated human mesenchymal stem cells obtained from cord blood as taught by either Bruder et al or Abatangelo et al. would have the same immunophenotypic characteristics as those of human USSCs in the present invention, such as **they are positive for CD29**, CD49e, CD44, CD54, **CD13**, CD90, SH2, SH3 and SH4 antigens and **negative for CD45**, CD34, **CD14**, HLA-DR, CD31, CD51/61, CD49d, CD`106 and CD64 as evidenced by the teachings of Ha et al (US 2005/0118714, paragraph 0027). Please, also note that where, as here, the claimed

and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. See In re Ludtke. Whether the rejection is based on "inherency" under 35 USC 102, or "prima facie obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. In re Best, Bolton, and Shaw, 195 USPQ 430, 433 (CCPA 1977) citing In re Brown, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972).

An ordinary skilled artisan would have been motivated to carry out the above modification because both Bruder et al and Abatangelo et al. already taught that isolated cord blood mesenchymal stem cells are suitable for therapeutic applications in a patient in need thereof.

An ordinary skilled artisan would have a reasonable expectation of success in light of the teachings of Pittenger et al., and either Bruder et al or Abatangelo et al., with a high level of skill of an ordinary skilled artisan in the relevant art.

Therefore, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Response to Arguments

Applicant's arguments related to the above new rejection in the Amendment filed on 4/7/08 (pages 3-4) have been fully considered, but they are respectfully not found to be persuasive for the following reasons.

1. The examiner notes that Applicant's arguments refer to Erices. However, Erices is not part of the above 103 rejection.

2. Applicant continues to argue basically that the claimed invention was not obvious and that Pittenger contains nothing that would have provided a reasonable likelihood of success. Applicant also argues that the field of using cells to teat a medical condition is unpredictable and the likelihood of success varies inversely with unpredictability. Applicant further refers the examiner to the Nussbaum article in which the authors observed the medically disastrous formation of a tetratoma rather than cardiac muscle repair using embryonic stem cells. Applicant also refers the examiner to the post-filing art of Mareschi to argue the point that there was still disagreement in the art about whether cord blood mesenchymal stem cells even existed, much less whether they could be administered in a manner similar to that described for bone marrow mesenchymal stem cells. Finally, Applicant argues that the experiment had to be performed because success could not have been predicted for achieving cardiac muscle repair.

Firstly, please note that that Pittenger describes the use of human mesenchymal stem cells derived from any source, **not necessarily limited only to human bone-**

marrow mesenchymal stem cells, for cardiac muscle regeneration. Please also see allowed claims issued in US 6,387,369 which is based on identical teachings of WO 99/03973.

Secondly, with respect to the issue whether the Bruder reference or the Abatangelo reference is enabled for the isolation of cord blood mesenchymal stem cells, the examiner already noted that similar isolation protocol is used for the preparation of MSCs derived from various tissue sources (e.g., bone marrow, cord blood and others) and USSCs. The isolation protocol comprises a density centrifugation gradient step, collecting mononuclear cell fraction, culturing and selecting adherent cells. Furthermore, various references already demonstrated that human mesenchymal stem/progenitor cells were successfully isolated from cord blood as evidenced at least by the prior art teachings of Alfonso et al. (Abstract #3897; IDS), Erices et al. (British Journal of Haematology 109:235-242; IDS), Abatangelo et al. (US 6,482,231; **see issued claims**), as well as post-filing art teachings of Goodwin et al. (Biology of Blood and Marrow Transplantation 7:581-588, 2001; IDS), Sandberg et al. (US 2004/0197310 A1 with an effective filing date of 2/12/2003) and Ha et al. (US 2005/0118714, paragraph 0027). Accordingly, there is nothing unpredictable about the use of mesenchymal stem cells derived from any sources, **particularly from bone marrow and/or from cord blood (USSCs)**, to treat a cardiac muscle disease in a human patient in need thereof in light of the teachings of Pittenger et al., with either Bruder et al or Abatangelo et al., coupled with a high level of skill of an ordinary skilled artisan in the relevant art.

Thirdly, with respect to the Nussbaum article it is not a surprise or unpredictable that transplanted ES cells in mice would result in the formation of tetratoma because it is widely known that ES cells are capable of forming tumors *in vivo*. Moreover, it is not a fair comparison between the totipotent ES cells and somatic stem cells such as mesenchymal stem cells because they are clearly distinct cells with clearly different properties.

Fourthly, with respect to the post-filing art of Mareschi the examiner is not convinced that there was a disagreement in the art whether blood cord mesenchymal stem cells even existed, particularly in light of the teachings of Erices et al., Abatangelo et al., Goodwin et al., Sandberg et al., and Ha et al. as already cited above.

Fifthly, once again there is nothing that is unpredictable on the regeneration of cardiac muscle in a human in need thereof **using human mesenchymal stem cells derived from bone-marrow or from blood cord (USSCs of the present invention)**.

Accordingly, claims 1-2 are still rejected under 35 U.S.C. 103(a) as being unpatentable over Pittenger et al. in view of either Bruder et al. or Abatangelo et al. as evidenced by Ha et al. for the same reasons already set forth in the above rejection.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Quang Nguyen, Ph.D., whose telephone number is (571) 272-0776.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's SPE, Joseph T. Woitach, Ph.D., may be reached at (571) 272-0739.

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1633; Central Fax No. (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

/QUANG NGUYEN, Ph.D./
Primary Examiner, Art Unit 1633